

Please enter 55/ab 3/22/05

**AMENDMENT TO THE CLAIMS**

The present amendment cancels claims 1-3, 11, 12, 20-24, 49 and 51 and amends claims 4-10, 13, 14, 16, 18, 19, 25-28, 32, 43, 44, 50, 53 and 54. According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the following claims are in the case:

- 7 / 4. (Currently Amended) The kit of claim <sup>1</sup> ~~52~~, wherein said targeting agent-therapeutic agent construct comprises at least a first anti-aminophospholipid antibody that binds to phosphatidylethanolamine, or antigen-binding fragment thereof.
- 8 / 5. (Currently Amended) The kit of claim <sup>7</sup> ~~4~~, wherein said targeting agent-therapeutic agent construct comprises at least a first IgG or IgM anti-aminophospholipid antibody that binds to phosphatidylethanolamine.
- 9 / 6. (Currently Amended) The kit of claim <sup>7</sup> ~~4~~, wherein said targeting agent-therapeutic agent construct comprises at least a first scFv, Fv, Fab', Fab or F(ab')<sub>2</sub> antigen-binding fragment of an anti-aminophospholipid antibody that binds to phosphatidylethanolamine.
- 10 / 7. (Currently Amended) The kit of claim <sup>7</sup> ~~4~~, wherein said targeting agent-therapeutic agent construct comprises at least a first recombinant anti-aminophospholipid antibody that binds to phosphatidylethanolamine, or antigen-binding fragment thereof.
- 11 / 8. (Currently Amended) The kit of claim <sup>7</sup> ~~4~~, wherein said targeting agent-therapeutic agent construct comprises at least a first human, humanized or part-human chimeric anti-

aminophospholipid antibody that binds to phosphatidylethanolamine, or antigen-binding fragment thereof.

<sup>12</sup> 9. (Currently Amended) The kit of claim <sup>7</sup>4, wherein said targeting agent-therapeutic agent construct comprises at least a first monoclonal anti-aminophospholipid antibody that binds to phosphatidylethanolamine, or antigen-binding fragment thereof.

<sup>13</sup> 10. (Currently Amended) The kit of claim 1, wherein said targeting agent-therapeutic agent construct comprises at least a first aminophospholipid binding protein that binds to phosphatidylethanolamine or an aminophospholipid-binding fragment thereof.

**Claims 11 and 12 cancelled**

<sup>14</sup> 13. (Currently Amended) The kit of claim <sup>13</sup>10, wherein said targeting agent-therapeutic agent construct comprises at least a first ~~Annexin V~~ or kininogen or ~~an aminophospholipid-binding~~ a phosphatidylethanolamine-binding fragment thereof.

<sup>15</sup> 14. (Currently Amended) The kit of claim <sup>1</sup>13, wherein said targeting agent-therapeutic agent construct comprises at least a first anticellular or cytotoxic agent.

<sup>16</sup> 15. (Original) The kit of claim <sup>15</sup>14, wherein said targeting agent-therapeutic agent construct comprises at least a first gelonin, ricin A chain or deglycosylated ricin A chain.

17  
16. (Currently Amended) The kit of claim + ~~52~~, wherein said targeting agent-therapeutic agent construct comprises at least a first coagulant.

18  
17. (Original) The kit of claim ~~16~~, wherein said targeting agent-therapeutic agent construct comprises at least a first Tissue Factor, dimeric Tissue Factor, trimeric Tissue Factor, polymeric Tissue Factor, mutant Tissue Factor, truncated Tissue Factor or a Tissue Factor derivative.

19  
18. (Currently Amended) The kit of claim + ~~52~~, wherein said targeting agent-therapeutic agent construct comprises an ~~anti-phosphatidylserine~~ antibody that binds to phosphatidylethanolamine, or antigen binding fragment thereof, ~~that~~ wherein said antibody or antigen binding fragment thereof is directly or indirectly attached to truncated Tissue Factor.

20  
19. (Currently Amended) The kit of claim + ~~52~~, wherein said kit comprises at least a first pharmaceutically acceptable formulation suitable for intravenous administration.

**Claims 20-24 cancelled**

21  
25. (Currently Amended) The kit of claim 24 ~~52~~, wherein said at least a first targeting agent-therapeutic agent construct and said at least a second anti-cancer agent are comprised within a single pharmaceutical composition.

22  
26. (Currently Amended) The kit of claim 24 ~~52~~, wherein said at least a first targeting agent-therapeutic agent construct and said at least a second anti-cancer agent are comprised within distinct pharmaceutical compositions.

23  
27. (Currently Amended) The kit of claim 24 ~~52~~<sup>1</sup>, wherein said at least a second anti-cancer agent is a chemotherapeutic agent, radiotherapeutic agent, anti-angiogenic agent or apoptosis-inducing agent.

24  
28. (Currently Amended) The kit of claim 24 ~~52~~<sup>1</sup>, wherein said at least a second anti-cancer agent is an antibody-therapeutic agent construct comprising a second targeting antibody, or antigen-binding fragment thereof, that binds to a surface-expressed, surface-accessible or surface-localized component of a tumor cell, tumor stroma or tumor vasculature; wherein said targeting antibody or fragment thereof is operatively linked to a therapeutic agent.

25  
29. (Original) The kit of claim 28<sup>24</sup>, wherein said second targeting antibody, or antigen-binding fragment thereof, binds to a surface-expressed, surface-accessible, surface-localized, cytokine-inducible or coagulant-inducible component of intratumoral blood vessels of a vascularized tumor.

26  
30. (Original) The kit of claim 29<sup>25</sup>, wherein said second targeting antibody, or antigen-binding fragment thereof, binds to a component of intratumoral vasculature selected from the group consisting of an aminophospholipid, endoglin, a TGF $\beta$  receptor, E-selectin, P-selectin, VCAM-1, ICAM-1, PSMA, a VEGF/VPF receptor, an FGF receptor, a TIE,  $\alpha_v\beta_3$  integrin, pleiotropin, endosialin, an MHC Class II protein, VEGF/VPF, FGF, TGF $\beta$ , a ligand that binds to a TIE, a tumor-associated fibronectin isoform, scatter factor/hepatocyte growth factor (HGF), platelet factor 4 (PF4), PDGF and TIMP.

27/

31. (Original) The kit of claim 28, wherein said second targeting antibody, or antigen-binding fragment thereof, is operatively linked to gelonin, deglycosylated ricin A chain, Tissue Factor, truncated Tissue Factor or to an antibody, or antigen-binding fragment thereof, that binds to Tissue Factor or truncated Tissue Factor.

24/

28/

32. (Currently Amended) The kit of claim 1 52, wherein said kit further comprises ~~biologically effective amounts of:~~

- (a) ~~said at least a first targeting agent therapeutic agent construct that comprises at least a first targeting agent that binds to an aminophospholipid operatively attached to at least a first therapeutic agent;~~
- (b) ~~said a targeting agent-detectable agent construct that comprises a second targeting agent that binds to an aminophospholipid~~ phosphatidylethanolamine ~~operatively attached to a detectable agent; and~~
- (c) ~~said at least a second anti-cancer agent.~~

**Claims 33-42 cancelled**

29/

43. (Currently Amended) In combination, biologically effective amounts of:

- (a) a first composition comprising at least a first anti-cancer agent, wherein said at least a first anti-cancer agent is at least a first targeting agent-therapeutic agent construct that comprises at least a first therapeutic agent operatively attached to at least a first targeting agent that binds to an aminophospholipid operatively attached to at least a first therapeutic agent phosphatidylethanolamine;

- (b) a second composition comprising a targeting agent-detectable agent construct that comprises a detectable agent operatively attached to a second targeting agent that binds to ~~an aminophospholipid operatively attached to a detectable agent~~ phosphatidylethanolamine; and
- (c) at least a second anti-cancer agent other than said at least a first targeting agent-therapeutic agent construct.

30/ 44. (Currently Amended) The kit of claim 20 <sup>29</sup>43, wherein the targeting agent of said at least a first targeting agent-therapeutic agent construct and the targeting agent of said targeting agent-detectable agent construct are anti-aminophospholipid antibodies that bind to phosphatidylethanolamine, or antigen-binding fragments thereof, obtained from the same antibody preparation or antibody-producing hybridoma.

31/ 45. (Previously Presented) The combination of claim <sup>29</sup>43, wherein said first composition is a pharmaceutical composition.

32/ 46. (Previously Presented) The combination of claim <sup>29</sup>43, wherein said second composition is a pharmaceutical composition.

33/ 47. (Previously Presented) The combination of claim <sup>29</sup>43, wherein said at least a second anti-cancer agent is admixed with said at least a first targeting agent-therapeutic agent construct to form a therapeutic cocktail.

34 / 48. (Previously Presented) The combination of claim 43, wherein said at least a second anti-cancer agent is comprised within a composition distinct from said at least a first targeting agent-therapeutic agent construct.

**Claim 49 cancelled**

35 / 50. (Currently Amended) The kit of claim + 52, wherein said kit comprises at least a first pharmaceutically acceptable liposomal formulation.

**Claim 51 cancelled**

52. (Previously Presented) A kit comprising, in a pharmaceutically acceptable form, therapeutically effective amounts of:

- (a) at least a first anti-cancer agent, wherein said at least a first anti-cancer agent is at least a first targeting agent-therapeutic agent construct that comprises at least a first targeting agent operatively attached to at least a first therapeutic agent, wherein said at least a first targeting agent binds to phosphatidylethanolamine expressed on the luminal surface of blood vessels of a vascularized tumor; and
- (b) at least a second anti-cancer agent other than said at least a first targeting agent-therapeutic agent construct.

2 / 53. (Currently Amended) A kit comprising, in a pharmaceutically acceptable form, therapeutically effective amounts of:

- (a) at least a first anti-cancer agent, wherein said at least a first anti-cancer agent is at least a first targeting agent-therapeutic agent construct that comprises at least a first targeting agent operatively attached to at least a first therapeutic agent, wherein said at least a first targeting agent binds to ~~an aminophospholipid~~ phosphatidylethanolamine on the luminal surface of blood vessels of a vascularized tumor; and
- (b) at least a second anti-cancer agent other than said at least a first targeting agent-therapeutic agent construct; wherein said at least a second anti-cancer agent:
  - (i) increases ~~aminophospholipid~~ phosphatidylethanolamine expression in the endothelium of said blood vessels of said vascularized tumor or injures or induces apoptosis in the endothelium of said blood vessels of said vascularized tumor; or
  - (ii) kills tumor cells of said tumor or is an anti-angiogenic agent that inhibits metastasis of tumor cells.

3 54. (Currently Amended) The kit of claim <sup>2</sup>53, wherein said at least a second anti-cancer agent increases ~~aminophospholipid~~ phosphatidylethanolamine expression in the endothelium of said blood vessels of said vascularized tumor or injures or induces apoptosis in the endothelium of said blood vessels of said vascularized tumor.

4 55. (Previously Presented) The method of claim <sup>3</sup>54, wherein said at least a second anti-cancer agent is taxol, vincristine, vinblastine, neomycin, a combretastatin, a podophyllotoxin, TNF- $\alpha$ , angiostatin, endostatin, vasculostatin, an  $\alpha_v\beta_3$  antagonist, a calcium-flux inducing agent, a calcium ionophore, H<sub>2</sub>O<sub>2</sub>, thrombin, an inflammatory cytokine or interleukin-4.



~~5~~ 56. (Previously Presented) The kit of claim ~~2~~ 53, wherein said at least a second anti-cancer agent kills tumor cells of said tumor or is an anti-angiogenic agent that inhibits metastasis of tumor cells.

~~6~~ 57. (Previously Presented) The kit of claim ~~5~~ 56, wherein said at least a second anti-cancer agent is an anti-tumor cell immunoconjugate, a chemotherapeutic agent or an anti-angiogenic agent.